HIGHLY DIASTEREOSELECTIVE SYNTHESIS OF POLYCYCLIC ALCOHOLS VIA ANIONIC CASCADE CYCLIZATION

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Polycyclic molecular architectures are the hallmark of many important bioactive natural products. The structural complexity of such compounds often represents a formidable challenge in their synthesis and requires multistep tedious procedures to ensure the correct installation of all stereogenic centers. On the other hand, cascade cyclization reactions where one step occurs after another along a well-defined sequence of events allows an access to complex polycyclic scaffolds in one-pot operation. The cation initiated cyclization cascades of unsaturated substrates are well known and widely utilized in both biological and synthetic setups, however, the corresponding anionic reactions are much less explored.

Herein we report a hitherto unknown cascade cyclization reaction representing the first example of formal [2+2] cycloaddition reaction between ketone enolates and allenes. The careful choice of base enables a well-orchestrated synthetic sequence via *in situ* formation of allene from the corresponding propargylic ethers. Subsequent addition of ketone enolate results in the formation of anionic intermediate which after intramolecular addition to carbonyl group affords unique polycyclic scaffold comprising of fused six-, five- and four-membered rings. The reaction is fully diastereoselective and allows the assembly of otherwise hardly accessible compounds possessing four consecutive quaternary carbons.

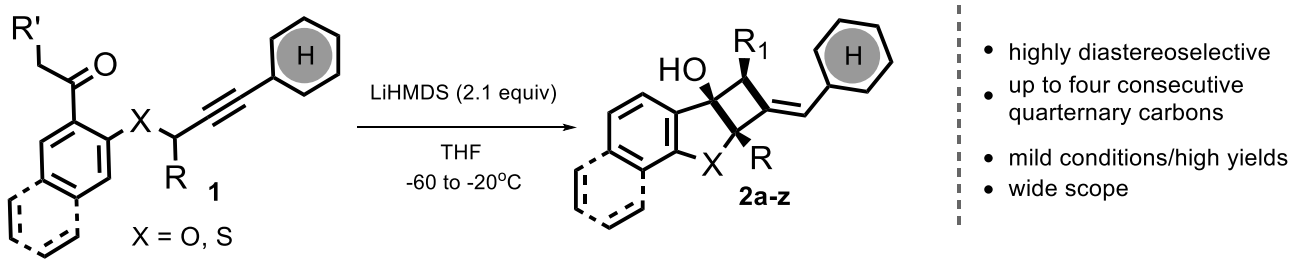

Fig. 1. Anionic cascade cyclization initiated by an addition of enolate to *in situ* formed allene.